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10/564,020	01/09/2006	Irene Bozzoni	2312.001US1	7176

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EXAMINER
CHONG, KIMBERLY

ART UNIT	PAPER NUMBER
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE <u>3</u> MONTH(S) OR THIRTY (30) DAYS,
WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.
- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed
  after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
  Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any
  earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on <u>23 April 2008</u>.

2a)☐ This action is **FINAL**.   2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is
closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) <u>1-7</u> is/are pending in the application.

    4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) <u>1-6</u> is/are rejected.

7)☒ Claim(s) <u>7</u> is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on <u>09 January 2006</u> is/are: a)☒ accepted or b)☐ objected to by the Examiner.

    Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

    Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

    a)☐ All   b)☐ Some * c)☐ None of:

      1.☐ Certified copies of the priority documents have been received.

      2.☐ Certified copies of the priority documents have been received in Application No. _____.

      3.☐ Copies of the certified copies of the priority documents have been received in this National Stage
         application from the International Bureau (PCT Rule 17.2(a)).

    * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☒ Information Disclosure Statement(s) (PTO/SB/08)
    Paper No(s)/Mail Date <u>1/9/2006</u>.

4)☐ Interview Summary (PTO-413)
    Paper No(s)/Mail Date. _____.

5)☐ Notice of Informal Patent Application

6)☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-7, in the reply filed on 11/06/2007 is acknowledged.

Status of the Application

Claims 1-7 are pending and currently under examination.

Information Disclosure Statement

The information disclosure statement filed on 01/09/2006 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because of the following reasons:

The IDS has not been considered because the documents are not contained in the instant application. The IDS has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Claim Objections

Claim 7 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only and/or cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, claim 7 has not been further treated on the merits.

Specification: Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because throughout the entire specification, sequences are recited without the proper sequence identifiers.

A complete response to this office action must correct the defects cited above regarding compliance with the sequence rules and a response to the action on the merits which follows.

The aforementioned instance of failure to comply is not intended as an exhaustive list of all such potential failures to comply in the instant application. Applicants are encouraged to thoroughly review the application to ensure that the entire application is in full compliance with all sequence rules. This requirement will not be held in abeyance.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6 rejected under 35 U.S.C. 103(a) as being unpatentable over Kreutzer et al. (US 20040001811), Elbashir et al. (methods 2002, Vol. 26: 199-213), Hernandez (EMBO 1985, Vol. 4, No. 7: 1827-1837) and Skuzeski et al. (JBC 1984, Vol. 259, NO. 13: 8345-8352).

The instant claims are drawn to a recombinant vector for expression of a siRNA or miRNA comprising from 5' to 3' an RNA polymerase II promoter sequence from the U1 snRNA gene, suitable restricts sites for cloning, a sequence transcribing a pre-siRNA comprising an A or G residue, a sequence from 21 to 23 nucleotides corresponding to a sense region of a mRNA, a loop region, a sequence from 21 to 23 nucleotides corresponding to the antisense region, two final UU 3' overhang nucleotides and a termination sequence derived from the sequence at the 3' end of the gene for U1 snRNA, wherein the cloning site for the 5' end of the sequence is Bgl II, wherein the sequence has the structure as recited in claims 3 and 4, wherein the termination sequence is SEQ ID No. 18 as recited in claim 5 and wherein the promoter is inducible.

Kreutzer et al. teach the use of dsRNA for inhibition of expression of target genes and teach the dsRNA comprising a sense and antisense strand of 19-24 nucleotides in length, preferably 21 to 23 nucleotides in length with 3' overhang regions of 1-4

nucleotides (see paragraph 0033). In the sequence listing, Kreutzer et al. exemplifies

dsRNAs wherein the 5' nucleotide begins with a G nucleotide. Kreutzer et al. teach the

dsRNA can be expressed from an expression vector wherein the dsRNA is transcribed

by promoter and expressed as an inverted repeat joined by a linker polynucleotide such

that the dsRNA has a stem and loop structure (see paragraph 0087). Kreutzer et al.

teach the use of U1 snRNA pol II promoters, wherein the promoter is inducible (see

paragraphs 0089 and 0090).

Kreutzer et al. do not teach dsRNA specifically comprising UU 3' overhangs, the

use of termination sequences derived from the 3' end of the U1 snRNA sequence nor

teach specifically teaching a Bgl II cloning site.

Elbashir et al. teach the basic protocol for selection of siRNA sequences that can

be targeted to any gene and specifically teach siRNA comprising 3' overhang regions

comprising two U nucleotides and wherein the 5' end begins with an A nucleotide (see

page 202).

Nielson et al. teach the use of an expression vector for expressing small

inhibitory RNAs, such as antisense and ribozymes, comprising U1 snRNA pol II

promoters and teach such expression units preferably comprising a termination

sequences (see entire column 13, especially line 50-53).

Henderson teach that formation of the 3' end of mature transcripts synthesized

by a U1 snRNA RNA pol II promoter is directed by specific conserved U1 snRNA

sequences located at the 3' end, which comprises the claimed termination sequence

having SEQ ID No. 18 (see Figure 5).

Skuzeski et al. teach identification of essential regions of the U1 siRNA promoter

that are required for transcription initiation (see Abstract). Region -105 to -6 was

identified to be essential for proper initiation of transcription from the U1 promoter (see

page 8351 to 8352) and in order to clone this region into an appropriate vector, the

HU1-1 gene should be digested with a Bgl II enzyme which cleaves the gene at position

-6 (see Figure 5 and page 8346 column 1).

It would have been obvious to one of ordinary skill in the art to make a siRNA

comprising 3' UU overhangs as taught by Elbashir et al. and include a termination

sequence, as taught by Henderson, into the expression vector as claimed. It would

have further been obvious to clone the U1 snRNA promoter into the expression vector

using a Bgl II restriction site for the reasons taught by Skuzeski et al.

One of ordinary skill in the art would have looked to Elbashir et al. while making a

siRNA as taught by Kreutzer et al. in order to design the optimal siRNA which includes

3' UU overhangs given it was well known in the art that Elbashir et al. provides the rules

for construction of siRNA. Further, one of ordinary skill in the art would have wanted to

use a termination sequences in an expression construct given Nielson et al. teach such

sequences are preferred when constructing an expression vector to express inhibitor

RNAs. One of ordinary skill in the art would have wanted to use the 3' end of a U1

snRNA promoter as a termination sequence given Henderson teach specific conserved

sequences of the 3' end of the U1 snRNA gene is required for formation of mature

transcripts by a U1 snRNA promoter. The benefits of construction expression vectors

comprising U1 snRNA promoters and the required 3' U1 snRNA gene termination

sequences are well known in the art as well as expression of therapeutic RNAs such as antisense and ribozymes using U1 snRNA pol II promoters and one would have wanted to use the required termination sequences to efficiently express the siRNAs from the vector taught by Kreutzer and would have expected to be able to incorporate a Bgl II site at the 5' end of an expression vector.

Moreover, given that is was well known in the art about the essential regions required for transcription initiation using a U1 snRNA promoter, as demonstrated by Skuzeski et al., one of ordinary skill in the art would have generated a Bgl II cloning site at the 5' end of a construct to efficiently be able to clone the required regions as taught by Skuzeki et al. One of ordinary skill in the art would have wanted to use a Bgl II cloning site to be able to clone in the required region to restore this region to the wild-type sequence to be able to initiate transcription of a siRNA sequence.

One of ordinary skill in the art would have expected to be able to incorporate two U nucleotides at the 3' end of the siRNA given Kreutzer et al. teach dsRNA with 3' overhangs and given Elbashir et al. teach the basic steps in designing such an siRNA sequence. One would have further expected to be able to incorporate the 3' termination sequence of the U1 snRNA gene into a construct comprising a U1 promoter because Henderson has demonstrated this sequence works to create mature 3' end transcripts from an expression vector comprising a U1 promoter.

Thus in the absence of evidence to the contrary, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Kimberly Chong/
Examiner
Art Unit 1635